Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-3 (cancelled)

Claim 4 (previously amended): A method as claimed in claim 38, wherein vascular collateralization of the embolized vasculature is absent or sufficiently delayed such that said composition is therapeutically effective.

Claim 5 (previously amended): A method as claimed in claim 38, wherein said non-polymeric particulate matrix comprises an insoluble phosphate salt of the formula

$$M_{10}(PO_4)_6A_z$$

wherein

M = Ba, Ca, Cd, Mg, Pb or Sr

A = OH^-, Cl^-, F^- or CO_2^{-2}

Z = 2 if A is univalent, 1 if A is divalent.

Claim 6 (previously amended): A method as claimed in claim 5, wherein said insoluble phosphate salt is hyroxyapatite, $Ca_{10}(PO_4)_6OH_2$.

Claim 7 (cancelled)

8. (withdrawn) A method of radiation therapy of a tissue comprising the steps of:

i) administering into the vasculature including the capillaries of a perfused zone of tissue in a human or non-human animal subject a composition comprising particles of a size or formulation selected to generate emboli at a target site within said subject, characterised in that as said particles are used solid water-insoluble particles 1-50 micrometers in size of a non-radioactive diagnostically effective compound in a non-polymeric particulate matrix selected from the group consisting of insoluble metal oxides, insoluble metal salts, inert metals, glass, ceramic particles and porous particles or vesicles encapsulating a non-radioactive diagnostically effective compound or a solution thereof; and

ii) applying a therapeutic dose of radiation, wherein said particles act as a radiation therapy sensitizer.

9. (withdrawn) A method as claimed in claim 8, wherein said composition further comprises a conventional contrast agent.

10. (withdrawn) A method as claimed in claim 8, wherein said conventional contrast agent acts as a radiation therapy sensitizer.

11. (withdrawn) A method as claimed in claim 8, wherein said therapeutic dose of radiation originates from a source external to said tissue.

12. (withdrawn) A method as claimed in claim 8, wherein said therapeutic dose of radiation originates from a source internal to said tissue.

13. (withdrawn) A method as claimed in claim 8, wherein said internal source of radiation comprises implanted ^{125}I.

14. (withdrawn) A method as claimed in claim 8, wherein said conventional contrast agent is a radio-dense material.

15. (withdrawn) A method as claimed in claim 8, wherein said radio-dense material comprises an iodinated contrast agent.

16. (withdrawn) A method as claimed in claim 8, wherein said iodinated contrast agent is selected from the group consisting of 6-(ethoxycarbonyl)hexyl bis(3,5-acetylamino)-2,4,6-triiodobenzoate (NC67722), (ethoxycarbonyl)methyl bis(3,5-acetylamino)-2,4,6-triiodobenzoate (NC12901), 1-(ethoxycarbonyl)pentyl bis(3,5-acetylamino)-2,4,6-triiodobenzoate (NC70146) and ethyl bis(3,5-acetylamino)-2,4,6-triiodobenzoate (NC8883).

17. (withdrawn) A method as claimed in claim 8, wherein said conventional contrast agent is both an MR active and X-ray absorbing material.

18. (withdrawn) A method as claimed in claim 8, wherein said conventional contrast agent is selected from the group consisting of gadolinium oxide, gadolinium oxalate and manganese-doped hydroxyapatite.

19. (withdrawn) A method of chemoembolic therapy comprising administering into the vasculature of a perfused zone of tissue in a human or non-human animal subject particles of a size or formulation selected to generate emboli at a target site within said subject, in combination with a therapeutic agent, characterised in that as said particles are used solid water-insoluble particles of a non-radioactive diagnostically effective compound or vesicles encapsulating a non-radioactive diagnostically effective compound or a solution thereof, and wherein said therapeutic agent is a promoter of vascular growth.

20. (withdrawn) A method of chemoembolic therapy comprising administering into the vasculature including the capillaries of a perfused zone of tissue in a human or non-human animal subject particles of a size or formulation selected to generate emboli at a target site within said subject, in combination with a therapeutic agent, characterised in that as said particles are used solid water-insoluble particles 1-50 micrometers in size of a non-radioactive diagnostically effective compound in a non-polymeric particulate matrix selected from the group consisting of insoluble metal oxides, insoluble metal salts, inert metals, glass, ceramic particles and porous particles or vesicles encapsulating a non-radioactive diagnostically effective compound or a solution thereof, and wherein said therapeutic agent is an inhibitor of vascular growth.

21. (withdrawn) A method as claimed in claim 19, wherein said promoter of vascular growth is selected from the list comprising vascular endothelial growth factor (VEGF), vascular endothelial growth factor-related protein, basic fibroblast growth factors (bFGF and

FGF-3), epidermal growth factor, hepatocyte growth factor, insulin-like growth factor, placental growth factor, placental proliferin-related protein, platelet-derived growth factor, platelet-derived endothelial growth factor, proliferin, proliferin-related protein, transforming growth factors α and β and tumor growth factor α.

22. (withdrawn) A method as claimed in claim 20, wherein said inhibitor of vascular growth is selected from the list comprising tecogalan sodium (Daiichi), AGM-1470 (Takeda/Abbott), CM101 (Carbomed), mitaflaxone (Lipha), GM-1603 (Glycomed), rPF4 (Repligen), MPF-4 (Lilly), recombinant angiostatin (Entremed), endostatin, thalidomide (Entremed), DC101 (ImClone Systems), OLX-514 (Aronex), raloxifene hydrochloride (Lilly), suramin sodium (Parke-Davis), IL-12 (Roche), marimastat (British Biotech), and CAI (NCI).

23. (withdrawn) A method as claimed in claim 19, wherein said therapeutic agent is a cytotoxin.

24. (withdrawn) A method as claimed in claim 19, wherein said cytotoxin is selected from the group comprising carboplatin, mitoxantrone, epirubicin, mitomycin C, decarbazine, vinblastine, cisplastin, interferon, dactinomycin, hydroxyurea, carmustine, methyl CNNU, interleukin-2, cyclophosphamide, amsacrine and doxorubicin.

25. (withdrawn) A method as claimed in claim 19, wherein said therapeutic agent is a biotherapeutic agent.

26. (withdrawn) A method as claimed in claim 19, wherein said biotherapeutic agent is selected from the group consisting of antisense nucleic acids, diphtheria toxin and ricin A chain.

27. (withdrawn) A method as claimed in claim 19, wherein said therapeutic agent is a nuclear agent.

28. (withdrawn) A method as claimed in claim 19, wherein said particles are administered prior to administration of said therapeutic agent.

29. (withdrawn) A method as claimed in claim 19, wherein said particles are administered after administration of said therapeutic agent.

30. (withdrawn) A method as claimed in claim 19, wherein said particles are coadministered with said therapeutic agent.

31. (withdrawn) A method as claimed in claim 19, wherein said generated emboli are temporary and said therapeutic agent is targeted.

32. (withdrawn) A method as claimed in claim 19, wherein said generated emboli are temporary and said therapeutic agent comprises genetic material.

33. (withdrawn) A method as claimed in claim 19, wherein said therapeutic agent is a material that enhances another therapeutic intervention.

34. (withdrawn) A method as claimed in claim 19, wherein said therapeutic intervention is hyperthermia or photolytic therapy.

35. (withdrawn) A method of identifying local pharmacokinetics in tissue comprising administering into the vasculature including the capillaries of a perfused zone of tissue in a human or non-human animal subject particles of a size or formulation selected to generate emboli at a target site within said subject optionally in combination with an imageable agent, characterised in that as said particles are used solid water-insoluble particles 1-50 micrometers in size of a non-radioactive diagnostically effective compound in a non-polymeric particulate matrix selected from the group consisting of insoluble metal oxides, insoluble metal salts, inert metals, glass, ceramic particles and porous particles or vesicles encapsulating a non-radioactive diagnostically effective compound or a solution thereof.

36. (withdrawn) Use of solid water-insoluble particles of a non-radioactive diagnostically effective compound or vesicles encapsulating a non-radioactive diagnostically effective compound or a solution thereof as defined in claim 1 for the manufacture of an embolus generating pharmaceutical composition for use in embolus therapy.

37. (withdrawn) A pharmaceutical composition comprising embolus forming contrast-effective particles together with a physiologically tolerable sterile liquid carrier medium, characterised in that as said particles are used solid water-insoluble particles of a non-

radioactive diagnostically effective compound or vesicles encapsulating a non-radioactive diagnostically effective compound or a solution thereof, as defined in claim 1.

Claim 38 (currently amended): A method of embolus therapy comprising the steps of: introducing into the vasculature of a human or non-human animal subject an embolus generating composition comprising particles of a size or formulation selected to generate emboli at a target site within said subject, wherein said embolus generating composition ~~includes~~ comprises solid water insoluble particles 10-20 micrometers in size consisting essentially of a water insoluble non-radioactive diagnostically effective compound encapsulated in a non-polymeric particulate matrix selected from the group consisting of insoluble metal oxides, insoluble metal salts, inert metals, glass, ceramic particles and porous particles, ~~or vesicles encapsulating a non-radioactive diagnostically effective compound, or a solution thereof,~~ and wherein said embolus generating composition further comprises an iodinated contrast agent, MR active agent, or ultrasound contrast agent imageable marker to identify the extent of embolization; and detecting the embolus location by a diagnostic imaging technique.

Claims 39-40 (cancelled)